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BIOCHEMICAL STUDIES IN DISEASES OF THE SKIN.
II. ACNE VULGARIS.

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THE theories of the causation of acne vulgaris are many and the remedial agents vary with the underlying notion of its etiology. The very fact that one dermatologist is convinced that it is an infectious disease, that another is certain that endocrinopathy is the causative factor, and that still a third is assured that some dietetic disturbance is responsible, is an evidence that our knowledge of the disease is vague. The changes in the chemistry of the body present in acne vulgaris deserve much study, for it appears to us that until the knowledge of the disturbance in metabolism of this condition is clear and definite, all theories of etiology and all plans of therapy are as fallacious as they are empiric.

It is the purpose of the present communication to summarize briefly the results that we have obtained in the study of some of the metabolic phases of the body in acne vulgaris. The work is still in progress and we hope to throw some more light on the subject in the future.

Nitrogen Retention Products in the Blood. In Table I, it will be observed that the urea nitrogen, non-protein nitrogen and creatinin content of the blood were determined in 12 cases. In general no abnormal figures were obtained. In those instances in which there were slight deviations from the normal figures, constitutional disorders like exophthalmic goiter and nephritis were found.

TABLE I.—NITROGEN RETENTION PRODUCTS IN THE BLOOD

Case.	Urea nitrogen.	Non-protein nitrogen.	Creatinin.
1	17	24	1.0
2	9	18	1.0
3	9	20	1.05
4	9	24	0.8
5	17	22	0.62
6	26	[illegible]	2.3
7	23	37	2.1
8	11	24	2.8
9	19	23	1.2
10	14	27	1.6
11	14	20	1.5
12	19	23	1.2

Calcium Content of the Blood. One year ago, Thro and Ehn reported that in acne vulgaris the calcium content of the blood (in 12 cases) showed a marked increase, the figures they obtained being from 13.6 mg. to 25.7 mg. per 100 cc of blood. In a previous paper we reported that we had failed to find an increase in the calcium content in the blood from 7 acne patients. At that time we employed the method of Halverson and Bergeim. During the past year we examined the blood from several patients with acne vulgaris for the calcium content by means of the method of Kahn and Hadjopoulus and again found no increase. Recently, Thro and Ehn reported that they found that they had used a faulty method in their previous communication. Upon using another they found quantities of calcium oxide in acne varying from 4.9 to 16.6 mg. per 100 cc of blood. They conclude, "We found that the calcium content of the blood was high in patients with very severe acne who had not been treated, but there were great variations in the amounts of calcium in the blood of acne patients."

The following method of Kahn and Hadjopoulos lends itself to the determination of calcium in small quantities of blood. By the use of this method we found no increase in the calcium content of the blood in acne cases:

To 1 cc of blood serum in a 10 cc test-tube add 4 cc of a 1 per cent solution of ammonium oxalate. Let stand for one-half to one hour and centrifuge for five minutes. Pour off the supernatant fluid. Wash the precipitate three times with distilled water, recovering the precipitate by means of centrifugalization. Add to the sediment 1 cc distilled water and transfer to a vitreosil crucible. The test-tube is washed with distilled water and the washings also collected in the crucible. The water is slowly evaporated and the precipitate burnt in a strong flame until calcium oxide is formed. Dissolve the ash in 0.5 cc fiftieth normal hydrochloric acid with hundredth normal sodium hydroxide, using phenolphthalein as an indicator. The amount of calcium oxide can now be calculated.

TABLE II.—CALCIUM CONTENT OF THE BLOOD IN ACNE VULGARIS

Case.	Mg. CaO in 100 cc.	Case.	Mg. CaO in 100 cc.
1	8.5	9	8.5
2	9.0	10	12.0
3	9.7	11	10.5
4	11.2	12	9.5
5	8.7	13	11.0
6	8.5	14	10.0
7	7.4	15	11.0
8	8.4		

Glycemia. Schwartz, Heimann and Mahnken reported that there is an increase in blood sugar in cases of acne vulgaris. In another communication describing our investigations on the blood chemistry in various skin diseases we corroborated the presence of a hyperglycemia or a high normal blood sugar content in acne. As shown in Table III, we have examined the blood from 34 patients during the postabsorptive period for the sugar content according to the method of Benedict. Out of the 34 specimens examined, 18, or almost 53 per cent, showed figures of 0.1 per cent or more; while 10 of these, or almost 23 per cent, showed figures of 0.12 per cent or more.

Glucose Tolerance. To 24 patients with acne vulgaris on a fasting stomach were administered 100 gm. of glucose in water. The blood was drawn from the vein previous to the administration of the glucose and subsequent to it at two intervals, one of forty-five minutes and the other of two hours. The blood was examined immediately for the glucose content in all these specimens. The results are recorded in Table III.

It will be seen that the glucose curve in all the cases is quite normal. In the average individual there is (subsequent to an ingestion of 100 gm. of glucose) a gradual rise in blood sugar, so that the maximum is attained after forty-five minutes. There is then a gradual decline to normal at the end of two hours. Patients who have a poor tolerance for carbohydrates will, on the other hand, show a continuous rise in the blood sugar with no decline in a period of several hours or days, and the glucose appears in the urine. This latter curve is most suggestive of early diabetes, hyperthyroidism being excluded.

In the series of 23 cases here reported the initial percentage of blood sugar varied from 0.058 to 0.135, rose to a height varying from 0.08 to 0.17 amd gradually receded to measurements ranging between 0.06 and 0.125, yielding curves corresponding to what we would call the normal.

Renal Glucose Threshold. It will also be observed that 4 of the patients (17, 21, 24 and 29) showed the presence of sugar in the urine subsequent to the ingestion of the glucose. The urine from all the 23 patients was examined for sugar prior to the administration of the glucose and at intervals of forty-five minutes and two hours subsequently. Sugar was absent from all the urines before and after the administration of the glucose, excepting in the specimens from the 4 patients mentioned above. The presence of glycosuria following the administration of 100 gm. of glucose; the presence of a normal blood-sugar curve, and the absence of other symptoms of diabetes warrant a diagnosis of decreased renal glucose threshold.

TABLE III.—GLYCEMIA, GLUCOSE TOLERANCE, RENAL GLUCOSE THRESHOLD IN ACNE VULGARIS

	GLYCEMIA, PER CENT.			
Case.	Prior to 100 gm. glucose ingestion.	After 3 to 4 hours.	After 2 hours.	Glucose in urine after test.
1	0.1			
2	0.09			
3	0.129			
4	0.13			
5	0.08			
6	0.13			
7	0.17			
8	0.2			
9	0.13			
10	0.1			
11	0.1			
12	0.08	0.088	0.085	0
13	0.08	0.09	0.07	0
14	0.058	0.08	0.06	0
15	0.07	0.09	0.07	0
16	0.08	0.095	0.07	0
17	0.08	0.1	0.09	+
18	0.07	0.15	0.08	0
19	0.06	0.08	0.07	0
20	0.12	0.16	0.09	0
21	0.135	0.165	0.1	+
22	0.07	0.09	0.06	0
23	0.07	0.85	0.06	0
24	0.11	0.17	0.09	+
25	0.06	0.095	0.07	0
26	0.1	0.15	0.1	0
27	0.12	0.17	0.13	0
28	0.09	0.14	0.12	0
29	0.09	0.16	0.1	+
30	0.12	0.15	0.13	0
31	0.11	0.15	0.125	0
32	0.09	0.17	0.1	0
33	0.1	0.13	0.09	0
34	0.1	0.16	0.135	0

Acidosis. In 1919, collaborating with Schwartz and Mahnken, we concluded as a result of investigations as to the alkali reserve of the blood in 139 skin cases that a mild or moderate state of acidosis had been found sufficiently often in acne vulgaris to warrant further study. Sweitzer and Michelson, in 1920, found no marked or consistent change in the alkali reserve in this condition. They employed the Van Slyke method for determining the carbon dioxide combining power of the plasma in 6 cases, and in only 1 was there a mild acidosis. Since then we have continued our studies on acidosis in acne vulgaris in 34 cases.

In this series there was only 1 case which showed a severe acidosis. In this girl the carbon dioxide combining power of the blood plasma was 36 per cent by volume, as determined by Van Slyke's method, and the alveolar carbon dioxide was 4.6 per cent as measured by Fredricia's apparatus. The ammonia output in the twenty-four-hour urine specimen was rather high, 2.74 gm. Ten of the other patients showed a mild acidosis as determined by these methods. Several of the remaining cases showed figures of a low normal alkali reserve of the blood bordering on an acidosis.

TABLE IV.—ACIDOSIS IN ACNE VULGARIS

Case.	CO_2 blood.	CO_2 alveolar Air.	NH_3 gm. 24-hr. urine.	Case.	CO_2 blood.	CO_2 alveolar air.	NH_3 gm. 24-hr. urine.
1	50	...	....	18	56	5.3	1.3
2	54	...	....	19	..	5.2	1.63
3	54	...	....	20	62	5.6	0.95
4	46	...	....	21	..	6.0	0.86
5	40	...	....	22	..	5.8	0.75
6	68	...	....	23	56	5.8	
7	66	...	....	24	54	5.6	
8	54	...	....	25	66	5.8	1.75
9	61	...	....	26	48	5.6	2.23
10	52	...	....	27	50	5.6	1.85
11	48	...	....	28	52	5.8	1.34
12	61	...	....	29	48	5.4	1.27
13	58	5.6	0.94	30	52	5.8	1.65
14	53	5.7	0.11	31	58	6.2	
15	62	5.8	1.51	32	55	5.6	1.53
16	60	5.5	0.82	33	..	5.2	2.25
17	50	5.4	0.82	34	36	4.6	2.74

Studies of the Feces. The stool from 23 patients was examined for enzymes, reaction, fermentation and microscopically for food fibers. It will be seen that most feces were acid in reaction and showed marked carbon dioxide fermentation. Only 4 gave ammoniacal fermentation. The enzymes were excellent in all cases for amylase, were good in all cases save 4 for protease, and were fair or good in all cases for lipase.

TABLE V.—FECES IN ACNE VULGARIS

			Enzymes			
Case.	Reaction.	Amylase.	protease.	Lipase.	Fermentation.	Food.
1	Acid	Good	Good	Good	CO_2	Meat and vegetable.
2	Acid	Good	Good	Good	CO_2	Meat and vegetable.
3	Acid	Good	Good	Good	CO_2	Meat and vegetable.
4	Acid	Good	Good	Good	CO_2	Meat and vegetable.
5	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
6	Alkaline	Good	Poor	Good	NH_3	Much meat.
7	Neutral	Good	Fair	Good	NH_3	Much meat.
8	Acid	Good	Good	Good	CO_2	Meat and vegetable.
9	Acid	Good	Good	Good	CO_2	Meat and vegetable.
10	Acid	Good	Good	Good	CO_2	Meat and vegetable.
11	Acid	Good	Good	Good	CO_2	Meat and vegetable.
12	Acid	Good	Good	Good	CO_2	Meat and vegetable.
13	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
14	Acid	Good	Good	Good	CO_2	Meat and vegetable.
15	Acid	Good	Good	Good	CO_2	Meat and vegetable.
16	Acid	Good	Good	Good	CO_2	Meat and vegetable.
17	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
18	Acid	Good	Good	Fair	CO_2	Meat and vegetable.
19	Neutral	Good	Fair	Fair	NH_3	Much meat.
20	Alkaline	Good	Poor	Fair	NH_3	Much meat.
21	Acid	Good	Good	Fair	CO_2	Vegetable.
22	Acid	Good	Good	Fair	CO_2	Vegetable.
23	Acid	Good	Good	Good	CO_2	Meat and vegetable.

The Basal Metabolism in Acne Vulgaris. Magnus-Levy was the first to point out the theoretical possibilities of metabolimetry in the diagnosis and treatment of constitutional disorders. It remained for DuBois and Benedict and others in this country to succeed in making data concerning the rate of energy production of distinct clinical importance. The term "basal metabolism" designates the heat production of an individual at the lowest level of cell chemistry. The heat production is at its minimum while the individual is at complete mental and physical rest. The most practical method for determining the heat production is by measuring the amount of oxygen consumption by means of a Benedict metabolimeter, and from these data the heat production is calculated in relation to the body surface, which is determined by Du Bois's height-weight chart. The caloric value of oxygen is employed to estimate the respiratory quotient obtained. A variation of 10 per cent from the average is considered within the normal limit.

In view of the fact that acne vulgaris is generally regarded as a cutaneous complication of a constitutional disorder, and considered by some dermatologists as depending for its etiology on an endocrinopathy, we deemed it advisable to determine the metabolic rate in a series of cases. From the data that we have obtained the metabolic rate in the average acne case seems to be enhanced. To incriminate the thyroid from this alone, however, is not justifiable, for the increase in oxygen consumption is very moderate. We hope in the near future to make other endocrine studies with the aim of throwing more light on the subject.

TABLE VI.—BASAL METABOLISM IN ACNE VULGARIS

Case.	Per cent.
1	+4
2	+5
3	−3
4	+10
5	+8
6	+9
7	+8
8	+6
9	+14
10	+12
11	+11
12	−3
13	+12
14	+12
15	+10
16	+11
17	+8
18	+9
20	+12
21	+11
22	+8

Summary and Conclusions. 1. We have studied the biochemical status of 38 patients with moderate and severe acne vulgaris of one to fifteen years' duration.

2. In 15 cases in which the nitrogen retention products in the blood were investigated no constant defect could be detected.

3. The calcium content of the blood in our series of cases was not increased.

4. Hyperglycemia, or a high normal blood sugar, accompanied over 50 per cent of the 34 cases studied.

5. The blood-sugar curve was normal in all the 23 patients who were studied for their carbohydrate tolerance.

6. The renal glucose threshold was decreased in 4 out of 23 patients.

7. A mild form of acidosis was found in about 30 per cent of the 34 patients.

8. Feces from 19 out of 23 patients showed carbohydrate fermentation, while only 4 showed protein putrefaction. The enzymes were excellent in all cases for amylase, were good in all cases save 4 for protease and were good or fair in all cases for lipase.

9. The metabolic rate seems to be slightly increased in acne vulgaris.

10. The presence of hyperglycemia and the increased basal metabolic rate seem to point toward dysfunction of the thyroid as a possible causative factor. We believe, however, other glands also are at fault.

11. The following measures have proved valuable in the treatment of this condition: Reduction of the carbohydrates in the diet, gastro-intestinal supervision, administration of alkalies and organotherapy.

12. Thyroid in some cases caused the appearance of increased sympathicotonus and increased the severity of the cutaneous condition; occasionally it seemed to produce involution of the lesions.

13. The administration of ovary, lutein and pituitary has been of benefit in some cases.